Endoscopic Vitrectomy Improves Outcomes of Seoul-type Keratoprosthesis Exchange in Rabbit Model

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PURPOSE. To investigate the efficacy of an endoscopic vitrectomy in Seoul-type keratoprosthesis (S-Kpro) exchange procedures.

METHODS. Nine S-Kpro-implanted rabbit eyes were enrolled in the S-Kpro exchange. Six eyes underwent an antecedent vitrectomy by an endoscopic system and then the S-Kpro exchange (endoscopy group). In the other three eyes, previously placed S-Kpros were removed, and a conventional vitrectomy was performed using the Eckardt keratoprosthesis, followed by an implantation of new S-Kpros (Eckardt group). All eyes were evaluated with slit lamp biomicroscopy and ultrasonography weekly to evaluate the time up to the development of the total retinal detachment (RD).

RESULTS. Vitreous traction membranes were found around the prosthesis of the exchange sites in all the S-Kpro-implanted rabbits; they were excised precisely through an endoscopic view in the endoscopy group. The mean survival time up to the RD development was 9.75 ± 4.70 weeks in the endoscopy group. In contrast, total retinal detachment or dialysis over 180° developed during surgery in all three eyes in the Eckardt group.

CONCLUSIONS. Antecedent endoscopic vitrectomy was safe and effective for the S-Kpro exchange in a rabbit model by removing the vitreous traction near the haptics before the exchange procedures. (Invest Ophthalmol Vis Sci. 2008;49:4407–4411) DOI:10.1167/iovs.08-1802

The Seoul-type keratoprostheses (S-Kpro) was designed for the treatment of severe intractable ocular surface diseases such as ocular cicatricial pemphigoid, chemical burns, and Stevens-Johnson syndrome.1 The design of the S-Kpro includes a double-fixation in which the cornea and sclera to improve the mechanical stability.2,3

In a clinical trial evaluating nine patients, S-Kpro implantation achieved favorable medium-term visual rehabilitation with long-term anatomic stability.4,5 However, retinal detachment (RD) occurred in all cases who had undergone the S-Kpro exchange procedures, whereas there was no RD after the primary implantation. The reason for the development of RD after the S-Kpro exchange is still unclear. It may be assumed that the vitreous traction was not relieved perfectly around the haptics during the exchange procedures.

Recently, Ray et al.6 reported that a modified vitreoretinal surgical technique could be used safely and effectively to treat posterior segment complications in patients with Dohlman-Doane keratoprosthesis. However, in the S-Kpro implanted eyes, conventional vitrectomy is difficult to perform, because the surgical field is limited by the long cylinder optics of the S-Kpro.

The purpose of this study was to evaluate the efficacy of an endoscopic vitrectomy for S-Kpro exchange procedures in rabbit eyes.

MATERIALS AND METHODS

This study was approved by the Institutional Animal Care and Use Committee of the Seoul National University Hospital, and performed according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. New Zealand White male rabbits were used for the experiments (weight: 2.5 to 3.5 kg). They were housed in rooms with ordinary fluorescent lamps (12 hours on, 12 hours off) and a room temperature of 21°C.

The S-Kpro was implanted in the right eyes of the rabbits as described elsewhere.1,5

The mean time for the exchange was 7.5 ± 4.0 weeks after the primary S-Kpro implantation and the eyes with RD, after the primary implantation, were excluded from this study; the time was not significantly different between the two groups (6.5 ± 6.1 weeks in endoscopy group, 8.0 ± 3.2 weeks in Eckardt group). The exchange procedures were performed by two methods. In the endoscopy group, an antecedent vitrectomy by endoscopy (E2 MicroProbe system; EndoOptics, Little Silver, NJ) was performed before the S-Kpro exchange. In the Eckardt group, a previously placed S-Kpro was removed, followed by a conventional vitrectomy using an Eckardt temporary keratoprosthesis, and then, a new S-Kpro was reimplanted. All procedures were performed on the right eyes of the rabbits. One experienced retinal surgeon performed the vitrectomy procedures. Although masking could not be used in this study, two investigators evaluated the rabbit eyes for the presence of RD separately during and after surgery.

Vitrectomy Using an Endoscope and the S-Kpro Exchange

Before surgery, ciprofloxacin hydrochloride 3 mg/mL eye drops and combination eye drops with phenylephrine hydrochloride 5 mg/mL and tropicamide 5 mg/mL were instilled in the eyes three times at 5-minute intervals. For anesthesia, we injected 0.5 mL of xylazine hydrochloride 23.3 mg/mL (Rompun; Bayer Korea Ltd., Seoul, Korea) and 0.5 mL of a combination anesthetic drug with tiletamine 125,

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mg/mL and zolazepam 125 mg/mL (Zoletil; Virbac, Carros, France) intramuscularly.

After a 360° conjunctival peritomy, a Flieringa fixation ring (Storz, St. Louis, MO) was placed onto the sclera 2 to 3 mm away from the limbus with a 6-0 black silk suture (Mersilk; Ethicon, Johnson & Johnson, Somerville, NJ; Fig. 1A). Then 6-0 polyglactin 910 (Coated Vicryl, Ethicon, Johnson & Johnson) sutures were preplaced and a sclerotomy for the infusion cannula was performed with an MVR blade 1 mm away from the limbus (Fig. 1B). The infusion cannula was introduced and sutured. We performed two additional sclerotomies for insertion of a vitreous cutter and an endoscopic probe (Fig. 1C). After adjustment of the orientation and focus, an endoscopic probe was introduced into the eyeball. (E) After completion of the vitrectomy, a skirt was incised near an optic, and the haptics were cut as peripherally as possible without any traction exerted. (F) Corneal lamellar dissection was performed, and the skirt was kept in the pocket. (G) After application of the corneal sutures, the infusion cannula was removed, and the sclerotomy was closed with the preplaced sutures.

FIGURE 1. Surgical procedure for the S-Kpro exchange in a rabbit model. (A) After conjunctival peritomy, a Flieringa ring was applied to the sclera. (B) After 6-0 polyglactin 910 sutures were preplaced, a sclerotomy for an infusion cannula was performed with an MVR blade 1 mm away from the limbus. (C) Two additional sclerotomies were performed for the insertion of a vitreous cutter and an endoscopic probe. (D) After adjustment of the orientation and focus, an endoscopic probe was introduced into the eyeball. (E) After completion of the vitrectomy, a skirt was incised near an optic, and the haptics were cut as peripherally as possible without any traction exerted. (F) Corneal lamellar dissection was performed, and the skirt was kept in the pocket. (G) After application of the corneal sutures, the infusion cannula was removed, and the sclerotomy was closed with the preplaced sutures.

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After a thorough vitrectomy, we closed the two sclerotomies used for the vitreous cutter and the endoscope. We injected viscoelastic agents into the vitreous cavity and removed the previously implanted keratoprosthesis. A previously formed lamellar pocket was reopened by dissection, adhesion of the skirt was relieved, and the skirt was incised near an optic with sharp scissors. The haptics were then cut as peripherally as possible without any traction exerted (Fig. 1E).

A new keratoprosthesis was placed into the eyeball, and 10-0 polypropylene sutures (Prolene; Ethicon, Johnson & Johnson), anchoring it in both haptics, were placed through the sclera from the inside out (ab interno technique). The new skirt was kept in the reopened lamellar pocket (Fig. 1F). Then, 8 to 10 corneal sutures were placed with 10-0 nylon to seal the corneal wound. The infusion cannula was removed, and the sclerotomy was closed with the preplaced sutures (Fig. 1G). The entire cornea, including the prosthesis, was covered with cryopreserved amniotic membrane to reduce inflammation and facilitate epithelialization. The conjunctival peritomy was repaired with 8-0 polyglactin sutures. We injected gentamicin sulfate 10 mg and

FIGURE 2. Microscopic intraocular findings during the endoscopic vitrectomy. (A) A core vitrectomy was performed in the mildly opacified vitreous, possibly resulting from the usual exaggerated fibrinoid reaction in rabbit eyes. (B) In the eyes with clear vitreous, triamcinolone-assisted vitrectomy can aid a more thorough vitreous removal. (C) Vitrectomy around the peripheral retina and vitreous base was performed with an improved view. (D, E) Careful removal of vitreous traction was performed around the haptics. (F) A small, latent hole was found in the retina after the core vitrectomy was completed (rabbit 7).
dexamethasone sodium phosphate 20 mg subconjunctivally. A bandage soft contact lens was applied with ofloxacin ointment 3 mg/g. A tarsorrhaphy was performed with a 6-0 black silk suture to prevent infection.

**Vitrectomy with the Eckardt Keratoprosthesis and S-Kpro Exchange**

Premedication, anesthesia, conjunctival peritomy, Flieringa ring fixation, and infusion cannula installation procedures were the same as just described. After viscoelastic agent injection, we removed the previously placed S-Kpro. An Eckardt temporary keratoprosthesis was inserted and sutured to the remnant peripheral cornea with four to eight 8-0 polyglactin sutures. We performed two additional sclerotomies for the insertion of the vitreous cutter and endoscopic probe. After turning off the lights from the microscope and room, we performed a core vitrectomy and a vitrectomy around the peripheral retina and vitreous base. After closing the sclerotomies, we removed the Eckardt keratoprosthesis and implanted a new S-Kpro. The rest of the procedure was the same as described earlier.

**Postoperative Management**

We applied ciprofloxacin hydrochloride 3 mg/mL and prednisolone acetate 10 mg/mL eye drops (Pred forte, Allergan, Irvine, CA) twice daily until 1 month after surgery. Then, ofloxacin 3 mg/g ointment and dexamethasone ointment with polymyxin B sulfate and neomycin sulfate (Maxitol; Alcon, Fort Worth, TX) were applied twice daily until the end of the follow-up period. Gentamicin sulfate 1 mg/kg was injected intramuscularly once a day. At each follow-up examination, for 2 months, we performed subconjunctival injection of gentamicin sulfate 10 mg, bandage soft contact lens exchange, and tarsorrhaphy repair to prevent infections.

**Follow-up**

During surgery, we evaluated the development of RD using endoscopy or an operating microscope. We examined the anterior segment and retina by slit-lamp biomicroscopy, indirect ophthalmoscopy and ultrasonography at 1, 2, 3, 4, 6, and 8 weeks and then, 3, 4, 5, and 6 months to evaluate the S-Kpro integrity, RD, endophthalmitis, and retropseudophthalmitic membrane formation. The rabbits were killed, and the right eyes were enucleated when total RD was confirmed or when the follow-up reached 6 months. We performed hematoxylin-eosin (H&E) staining on all specimens.

The time interval for up to total RD was defined as the time interval between surgery and the development of a funnel-shaped total RD, diagnosed by ultrasonography and was analyzed by Kaplan-Meier survival curves. The difference between the two groups was analyzed by the log rank test (SPSS ver. 12.0, SPSS, Chicago, IL). \( P < 0.5 \) was considered statistically significant.

**RESULTS**

The S-Kpro exchange procedure was performed in nine eyes. There were six eyes in the endoscopy group and three eyes in the Eckardt group. Neither endophthalmitis nor retropseudophthalmitic membrane formation occurred in this study. A spontaneous vitreous hemorrhage developed in one eye in the endoscopic group and spontaneously resolved during the follow-up. In another eye in the endoscopic group, an epiretinal membrane developed in the posterior pole. The surgical results of the nine eyes are summarized in Table 1.

In the endoscopy group, a total RD did not develop in two eyes until the last follow-up (rabbits 5 and 6). In one eye (rabbit 5), there were no specific findings during surgery, but a shallow RD was found during the first postoperative week. However, the RD was confined to the inferonasal area of the disc within the posterior pole (Fig. 3A) and did not progress to a total RD until the 26th postoperative week, when a dense epiretinal membrane combined with shallow RD was found on gross pathology and histology (Figs. 3B, 3C). In the other eye (rabbit 6), the retina was flat until the 17th postoperative week, but the rabbit died during the anesthesia and examination procedure (Figs. 3D–G).

A total RD developed in the other four eyes of the endoscopy group (rabbits 4, 7, 8, and 9). A funnel-shaped total RD developed during surgery in one eye (rabbit 4). In the other eyes (rabbits 7, 8, and 9), a shallow localized detachment was found during surgery and progressed to a total detachment at the second or third postoperative week. In rabbit 7, we found a silent retinal hole during surgery. We tried barrier laser treatment around the hole, but the procedure failed (Fig. 2F).

The mean survival time of the interval up to the total RD was 9.75 ± 4.70 weeks in the endoscopy group on Kaplan-Meier analysis (95% CI 0.53–18.97 weeks). In the Eckardt group, the total RD (rabbits 1 and 3) and retinal dialysis of 180° (rabbit 2) was found during the installation of the Eckardt keratoprosthesis after the S-Kpro was removed in all three eyes. The time interval up to the total RD was significantly prolonged in the endoscopy group, compared with the Eckardt group (\( P = 0.025 \)).

**DISCUSSION**

Since endoscopy with fiber optics was introduced to medical science in the 1960s, it has played an important role in almost all medical fields. However, endoscopy has not been widely used in ophthalmic surgeries, although it was attempted earlier for the removal of intraocular foreign bodies or for vitrectomy in eyes with media opacity. With the further development of...
endoscopic vitrectomy has been reported for an endoscope-guided photo-
thermal ablation of choroidal neovascular membranes, eva-
tuation of the peripheral retina and ciliary body, or vitrectomy in
eyes with media opacity.11–14

Currently, many surgeons use the temporary keratopro-
thesis such as the Eckardt keratoprosthesis for vitreo-retinal sur-
gery in eyes with corneal opacities.15 In those cases, vitrec-
tomy by endoscopy would be an another option.14 Thus, we
experimentally adapted these two methods, the vitrectomy
with the use of a temporary keratoprosthesis or an endoscopy,
to exchange the S-Kpro. As a result, we found that an endo-

endoscopic vitrectomy provided better outcome related to the ret-
ina. This result is likely to be clinically relevant, considering
that the outcomes after vitrectomy are poorer in rabbits than in
humans.16–19

Recently, the use of an endoscopic intraocular surgery has
been reported in four eyes with keratoprosthesis.10,20,21 One
eye with a Boston type I keratoprosthesis underwent vitrec-
tomy due to late-onset postoperative endophthalmitis, RD and
a thick retroprosthetic membrane.10 The other two eyes with
osteo-odonto-keratoprosthesis underwent vitrectomy because
of endophthalmitis or retinal redetachment after the removal
of silicone oil.20 Endoscopic cyclophotocoagulation was
performed on an eye with an osteo-odonto-keratoprosthesis
because thick buccal mucosa interfered with the accurate
localization of the ciliary body for transscleral cyclopho-
tocoagulation.21 Endoscopy seems to be useful in managing
postoperative complications after various keratoprostheses
were implanted. Our data support the efficacy of endoscopic
vitrectomy in S-Kpro-implanted eyes.

However, endoscopic vitrectomy has some disadvantages,
such as shallow depth perception, low resolution, difficulty
with control, and a long learning curve.10 These technical
problems are likely to improve with continued development of
better instruments in the near future.22

Half of the eyes in our study showed mild vitreous opacity
at the time of the exchange that seemed to result from com-
mon exaggerated fibrin reaction. This possibly occurred by
previous partial vitrectomy during the primary implantation.16
In the endoscopy group, this made the remnant vitreous
detectable more easily during the endoscopic vitrectomy. In
the eyes with clear vitreous, triamcinolone-assisted vitrectomy
aided the complete vitreous removal.23 With the help of an
endoscopy, we could see the retinal periphery and ciliary body
with an enhanced view as mentioned previously.13 Moreover,
by using the endoscope, we could easily identify the adhesive
membranes around the haptics of the S-Kpro as well as at the
scleral fixation sites, and subsequently removed the traction
effectively.

Van der Zee et al.17 reported that localized RD of the post-
erior retina developed in 16% of vitrectomized rabbit eyes
without any evidence of retinal holes. They proposed that the
vitreoretinal traction originated from fibrous proliferation into
the vitreous from the pars plana sclerotomy and was transmit-
ted to the posterior retina by the residual cortical vitreous. A
similar mechanism may explain our case with a localized RD in
the posterior pole (rabbit 5). A possible cause of the RD, in the
endoscopy group, might have been related to the inexperi-
enced surgical skill in using an endoscope, a retinal hole (rabbit
7), fluid from the region of the sclerotomy that could flow
towards the retina intraoperatively,17 and the severe dense
fibrin reaction caused by the long surgical time.17–19 We ex-
pect that improved surgical skill, a shorter surgical time, re-
duced fluid infusion flow, and heparin supplementation of the
infusion16 can lower the incidence of the postoperative RD
related to the S-Kpro exchange in the rabbit model. Moreover,
given that the RD occurs in rabbit more readily, endoscopic
vitrectomy in humans may be the most prudent step.

In the Eckardt group, a total RD and giant retinal dialysis
developed in three eyes. This may be due to the traction
membrane around the haptics and the posterior surface of
the S-Kpro not being fully removed before the S-Kpro explantation.

The small number of rabbits enrolled in this study limits the
interpretation of our findings. Nevertheless, this is the first
animal study on an endoscopic vitrectomy in keratoprothesis-
implanted eyes. The results suggest that an endoscopic vitrec-
tomy might be an option for retinal complications in human
keratoprosthetic eyes, and this article highlights the feasibility
of the endoscopic vitrectomy.
In conclusion, antecedent vitrectomy with an endoscopy improved the outcome of S-Kpro exchange by successfully removing vitreous traction near the scleral fixation sites. This approach may help to lengthen the survival of the implanted S-Kpro after exchange procedures.

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